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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/749,386	01/02/2004	Jian-Kang Zhu	247354US20DIV	9333

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EXAMINER
BAUM, STUART F

ART UNIT	PAPER NUMBER
1638	

NOTIFICATION DATE	DELIVERY MODE
12/12/2007	ELECTRONIC

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Notice of the Office communication was sent electronically on above-indicated "Notification Date" to the following e-mail address(es):

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Office Action Summary	Application No.	Applicant(s)	
	10/749,386	ZHU ET AL.	
	Examiner	Art Unit	
	Stuart F. Baum	1638	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *09 October 2007*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *36,43-46 and 51-61* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *36,43-46 and 51-61* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

RCE Acknowledgment

1. The request filed on 10/9/2007 for a Request for Continued Examination (RCE) under 37 C.F.R. § 1.114, based on parent Application No. 10/749,386 is acceptable and a RCE has been established. An action on the RCE follows.

2. Claims 36, 43-46, and 51-61 are pending and are examined in the present office action. The examination includes SEQ ID NO:1 encoding SEQ ID NO:2.

Claim Rejections - 35 USC § 112

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

3. Claims 43-45 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claims 43-45 are indefinite for reciting 70%, 80% and 90% identical to the sequence of SEQ ID NO:1, respectively. Claim 36, from which claims 43-45 are dependent, is drawn to a method comprising a polynucleotide encoding a polypeptide that is at least 95% identical to SEQ ID NO:2, which is 1146 amino acids. SEQ ID NO:1 is 6076 base pairs. A nucleic acid sequence that is 90% identical to SEQ ID NO:1, would encode a polypeptide that is at most 82% identical to SEQ ID NO:2 (6076 * 10% = 608; 608/3 (one codon) = 203; therefore, 203 amino acid changes); 1146 a.a. - 203 a.a. = 943 a.a.; 943 / 1146 = 0.82 which equals 82%). Therefore, it is

unclear how a sequence encoding a polypeptide having 95% identity to SEQ ID NO:2, can also have a sequence identity of 90% when compared to SEQ ID NO:1.

Written Description

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

4. Claims 43-45 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

The claims are drawn to a method of increasing the salt tolerance of a plant comprising increasing the expression of a polynucleotide encoding a polypeptide that is at least 95% identical to the amino acid sequence of SEQ ID NO:2, wherein said polynucleotide comprises a sequence that is at least 70%, 80% or 90% identical to SEQ ID NO:1.

Given the 112 second indefiniteness of the claims as discussed above, and for purposes of compact prosecution, the Office interprets the claims as if they are solely drawn to sequences that are at least 70%, 80% or 90% identical to SEQ ID NO:1 and do not encode a polypeptide that is at least 95% identical to the amino acid sequence of SEQ ID NO:2.

Applicants' invention is SEQ ID NO:1 (*SOS1*) encoding a Na^+/H^+ antiporter. Mutations in *SOS1* cause a salt-hypersensitive phenotype (page 15, 1st paragraph of "Results" section). *SOS1* was positionally cloned from *Arabidopsis* and is expressed constitutively through-out the

plant but is upregulated in response to NaCl treatment. The *Arabidopsis* genomic sequence of SOS1 is disclosed in Figures 7A-7D and corresponds to SEQ ID NO:1 and the encoded protein is disclosed in Figure 3A and corresponds to SEQ ID NO:2.

Applicants do not disclose a representative number of nucleic acid sequences that exhibit 70% sequence identity to SEQ ID NO:1 and encode a polypeptide with the same activity as the polypeptide encoded by SEQ ID NO:1.

The Federal Circuit has recently clarified the application of the written description requirement to inventions in the field of biotechnology. See University of California v. Eli Lilly and Co., 119 F.3d 1559, 1568, 43 USPQ2d 1398, 1406 (Fed. Cir. 1997). In summary, the court stated that a written description of an invention requires a precise definition, one that defines the structural features of the chemical genus that distinguishes it from other chemical structures. A definition by function does not suffice to define the genus because it is only an indication of what the gene does, rather than what it is. The court goes on to say, "A description of a genus of cDNAs may be achieved by means of a recitation of a representative number of cDNAs, defined by nucleotide sequence, falling within the scope of the genus or of a recitation of structural features common to members of the genus, which features constitute a substantial portion of the genus." *See University of California v. Eli Lilly and Co.*, 119 F.3d 1559; 43 USPQ2d 1398, 1406 (Fed. Cir. 1997).

Applicants fail to describe a representative number of polynucleotide sequences falling within the scope of the claimed genus of sequences that are at least 70% identical to SEQ ID NO:1. Applicants only disclose SEQ ID NO:1. Furthermore, Applicants fail to describe structural features common to members of the claimed genus of polynucleotides. Hence,

Applicants fail to meet either prong of the two-prong test set forth by *Eli Lilly*. Furthermore, given the lack of description of the necessary elements essential for the protein encoded by SEQ ID NO:1, it remains unclear what features identify an *Arabidopsis* SOS1 protein of SEQ ID NO:2. Since the genus of SOS1 proteins encoded by SEQ ID NO:1 has not been described by specific structural features, the specification fails to provide an adequate written description to support the breath of the claims.

Enablement

5. Claims 36, 43-46, and 51-61 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention.

The claimed invention is not supported by an enabling disclosure taking into account the *In re Wands* factors (858F.2d 731, 8 USPQ2d 1400 (Fed. Cir. 1988). *In re Wands* lists a number of factors for determining whether or not undue experimentation would be required by one skilled in the art to make and/or use the invention. These factors are: the quantity of experimentation necessary, the amount of direction or guidance presented, the presence or absence of working examples of the invention, the nature of the invention, the state of the prior art, the relative skill of those in the art, the predictability or unpredictability of the art, and the breadth of the claim.

The claims are drawn to a method of increasing the salt tolerance of a plant comprising increasing the expression of a polynucleotide encoding a polypeptide that is at least 95%

identical to the amino acid sequence of SEQ ID NO:2, wherein increasing the expression is by either increasing the copy number of said polynucleotide or by replacing the native promoter of said polynucleotide with a stronger promoter, or wherein said polynucleotide comprises a sequence that is at least 70%, 80% or 90% identical to SEQ ID NO:1, or wherein the polynucleotide comprises SEQ ID NO:1, or wherein the polynucleotide encodes the polypeptide of SEQ ID NO:2.

Given the 112 second indefiniteness of the claims as discussed above, and for purposes of compact prosecution, the Office interprets the claims as if they are solely drawn to sequences that are at least 70%, 80% or 90% identical to SEQ ID NO:1 and do not encode a polypeptide that is at least 95% identical to the amino acid sequence of SEQ ID NO:2.

Applicants' invention is SEQ ID NO:1 (*SOS1*) encoding a Na^+/H^+ antiporter. Mutations in *SOS1* cause a salt-hypersensitive phenotype (page 15, 1st paragraph of "Results" section). *SOS1* was positionally cloned from *Arabidopsis* and is expressed constitutively through-out the plant but is upregulated in response to NaCl treatment. *SOS1* mRNA is more abundant in roots than in shoots (page 17, 2nd paragraph). The Arabidopsis genomic sequence of SOS1 is disclosed in Figures 7A-7D and corresponds to SEQ ID NO:1 and the encoded protein is disclosed in Figure 3A and corresponds to SEQ ID NO:2.

Applicants have not reduced to practice their invention. Applicants have only used the *SOS1* nucleic acid to complement a *sos1* mutant, and one skilled in the art would not have a need to make a wild-type plant from a *sos1* mutant. Applicants disclose a method for increasing the salt tolerance of a plant comprising transforming a plant with the Applicants' invention (page 5, 1st full paragraph) but Applicants have not provided further guidance as to the spatial and

temporal expression that is required to achieve the desired result and Applicants have not reduced to practice any nucleic acid. Applicants disclose that their invention is a Na^+/H^+ antiporter. Shi et al (2000, PNAS 97(12):6896-6901) teach that anitporters require a proton motive force to be operable (page 6896, 2nd paragraph). Applicants have not taught whether the endogenous H^+ -ATPases would be sufficient to establish the proper H^+ gradient that would be required by the increased number of Na^+/H^+ antiporters that would comprise a plant transformed with Applicants' invention.

Applicants teach that *Arabidopsis* plants comprising a mutant *sos2* gene are less tolerant of high Na^+ environments or Na^+ / K^+ imbalances but Applicants have not taught increasing the expression of any SOS1 gene to produce a plant with increased salt tolerance. Larkin et al (1994, The Plant Cell 6:1065-1076) teach the unpredictability of transforming a plant to produce the opposite phenotype as the mutant-gene phenotype. Larkin et al teach that *GLABROUS1* (*GL1*) mutant plants have a reduced number of trichomes. Over-expressing GL1 in *Arabidopsis* does not produce plants with an increased number of trichomes compared to wild-type plants (page 1072, right column, 1st paragraph). Therefore, just because the *sos1* mutants exhibit an increased sensitivity to high Na^+ concentrations, does not mean that over-expressing *SOS1* will automatically produce plants with an increased tolerance to Na^+.

The state-of-the-art is such that one of skill in the art cannot predict which nucleic acids that encode a polypeptide that is at least 95% sequence identical to SEQ ID NO:2 will encode a protein with the same activity as a protein encoded by SEQ ID NO:1. The prediction of protein structure from sequence data and, in turn, utilizing predicted structural determinations to ascertain functional aspects of the protein, is extremely complex, and the positions within the

protein's sequence where amino acid substitutions can be made with a reasonable expectation of maintaining function are limited (Bowie et al, Science 247:1306-1310, 1990, see especially page 1306). Proteins may be sensitive to alterations in even a single amino acid in a sequence. For example, the replacement of a glycine residue located within the START domain of either the PHABULOSA or PHAVOLUTA protein receptor with either an alanine or aspartic acid residue, alters the sterol/lipid binding domain (McConnell et al, Nature 411 (6838):709-713, 2001, see especially page 710, left column, 2nd paragraph).

Applicants have not disclosed how one makes or isolates any of the sequences that are encompassed by Applicants' broad claims. Applicants have not taught which regions of the respective polynucleotides can be used to amplify any of said polynucleotides or which regions can be used as a probe to isolate any of said polynucleotide sequences.

In the absence of guidance, undue trial and error experimentation would be required for one of ordinary skill in the art to screen through the multitude of non-exemplified sequences, either by using non-disclosed fragments of SEQ ID NO:1 as probes or by designing primers to undisclosed regions of SEQ ID NO:2 and isolating or amplifying fragments, subcloning the fragments, producing expression vectors and transforming plants therewith, in order to identify those, if any, that when over-expressed increase the salt tolerance of a plant compared to a plant not transformed with said nucleic acid molecule.

Therefore, given the breadth of the claims; the lack of guidance and examples; the unpredictability in the art; and the state-of-the-art as discussed above, undue experimentation would be required to practice the claimed invention, and therefore the invention is not enabled.

The Office notes that Applicants' combined remarks concerning both sections of 112 first paragraph, written description and enablement, are written together and the Office addresses those remarks below.

Applicant's arguments filed 10/9/2007 have been fully considered but they are not persuasive.

Applicants contend that the degree of homology recited in the claims is consistent with the current position of the Office as manifest by a recent decision by the PTO's Board of Patent Appeals and Interferences in *Ex parte Bandman* (sentence bridging pages 6 and 7 of Remarks).

The Office contends the Board's opinion in *Ex parte Bandman* is non-precedential.

Applicants contend that claims drawn to a protein that is at least 95% identical to a disclosed sequence and has a specific function is within the guidelines set forth in the Written Description Guidelines (page 7 of Remarks, 1st full paragraph). The Guidelines state "There is actual reduction to practice of the single disclosed species" (page 7 of Remarks, 2nd full paragraph).

The Office contends Applicants have not disclosed an actual reduction to practice of any nucleic acid molecule. Applicants are invited to submit a 1.132 declaration.

Double Patenting

6. The nonstatutory double patenting rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or improper time wise extension of the "right to exclude" granted by a patent and to prevent possible harassment by multiple assignees. See *In re Goodman*, 11 F.3d 1046, 29 USPQ2d 2010

(Fed. Cir. 1993); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); *In re Van Ornum*, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970);and, *In re Thorington,* 418 F.2d 528, 163 USPQ 644 (CCPA 1969).

A timely filed terminal disclaimer in compliance with 37 CFR 1.321(c) may be used to overcome an actual or provisional rejection based on a nonstatutory double patenting ground provided the conflicting application or patent is shown to be commonly owned with this application. See 37 CFR 1.130(b).

Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b).

Claims 36, 43-46, and 51-61 are rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 8-11, 19-22, 29-33, 41-44, 52-55, 63-66 of U.S. Patent No. 6,727,408 B2. Although the conflicting claims are not identical, they are not patentably distinct from each other because the claims are obvious over the claims of Patent No. 6,727,408 B2.

The claims are drawn to a method of increasing the salt tolerance of a plant comprising increasing the expression of a polynucleotide encoding a polypeptide that is at least 95% identical to the amino acid sequence of SEQ ID NO:2, wherein increasing the expression is by either increasing the copy number of said polynucleotide or by replacing the native promoter of said polynucleotide with a stronger promoter, or wherein said polynucleotide comprises a sequence that is at least 70%, 80% or 90% identical to SEQ ID NO:1, or wherein the

polynucleotide comprises SEQ ID NO:1, or wherein the polynucleotide encodes the polypeptide of SEQ ID NO:2.

Given the 112 second indefiniteness of the claims as discussed above, and for purposes of compact prosecution, the Office interprets the claims as if they are solely drawn to sequences that are at least 70%, 80% or 90% identical to SEQ ID NO:1 and do not encode a polypeptide that is at least 95% identical to the amino acid sequence of SEQ ID NO:2.

Claims 8-11, 19-22, 29-33, 41-44, 52-55, 63-66 of U.S. Patent No. 6,727,408 B2 are drawn to a transgenic plant and method of making a transgenic plant comprising introducing an isolated polynucleotide comprising a nucleic acid sequence comprising SEQ ID NO:1 or encoding the polypeptide of SEQ ID NO:2. The Office contends Applicants' SEQ ID NO:1 exhibits 100% sequence identity with SEQ ID NO:1 from U.S. Patent No. 6,727,408 B2 (sequence search results previously submitted).

Though the claims are not identical, they are not patentably distinct because the claims of U.S. Patent No. 6,727,408 B2 are drawn to a method that is encompassed by the claims of the instant application and would produce a plant that has increased salt tolerance.

7. Claims 36, 43-46, and 51-61 are deemed free of the prior art, given the failure of the prior art to teach or reasonably suggest a method of increasing the salt tolerance of a plant in need thereof comprising increasing the expression of a polynucleotide encoding a polypeptide that is at least 95% identical to SEQ ID NO:2 wherein increasing the expression is by either increasing the copy number of said polynucleotide or by replacing the native promoter of said

polynucleotide with a stronger promoter, or wherein said polynucleotide comprises SEQ ID NO:1.

8. No claims are allowed.

9. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Stuart F. Baum whose telephone number is 571-272-0792. The examiner can normally be reached on M-F 8:30-5:00.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Anne Marie Grunberg can be reached at 571-272-0975. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is 571-272-1600.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

Stuart F. Baum Ph.D.
Primary Examiner
Art Unit 1638
November 29, 2007

STUART F BAUM, PH.D
PRIMARY EXAMINER